Located at the Harry S Truman Memorial Veterans' Hospital, the VA Biomolecular Imaging Center (BIC) offers VA and affiliated MU researchers state-of-the-art molecular and anatomic *in vivo* imaging capabilities. The imaging center houses a Siemens INVEON® small animal Micro-PET and a combined Micro-SPECT/CT, along with an actively shielded 7T MRI system employing a Bruker AVANCE III console and ParaVision® software (MRI system upgrade completed in 2013).

The primary purpose of the imaging center is to make high-resolution anatomic and molecular imaging capabilities readily available to MU and VA researchers who utilize conventional and immune-compromised animal models as a component of their respective research programs. These studies can be performed non-invasively allowing repeated measurements within the same research subject.

Multimodality imaging is often performed because of the value of both physiologic (PET and SPECT) and anatomic (CT and MRI) information from the same research subject. If requested by the researcher, reconstructed data from multiple modalities can be ported to a Microsoft Windows based system for visualization and image fusion.

The VA BIC is available to more than just the biomedical field. Researchers of various other areas have utilized the services of the VA BIC for analysis of a wide variety of materials. Micro-imaging can provide quantitative and qualitative information for items ranging from plants to engineering components.

In addition to the VA BIC imaging capabilities, the facility also has automated SPPS technology for the rapid synthesis of small peptides and automated radiolabeling technology for routine radiolabeling of biomolecules using positron and beta emitting radioisotopes for imaging and therapeutic research applications. The remaining pages provide technical information and applications for each aspect of our facility.

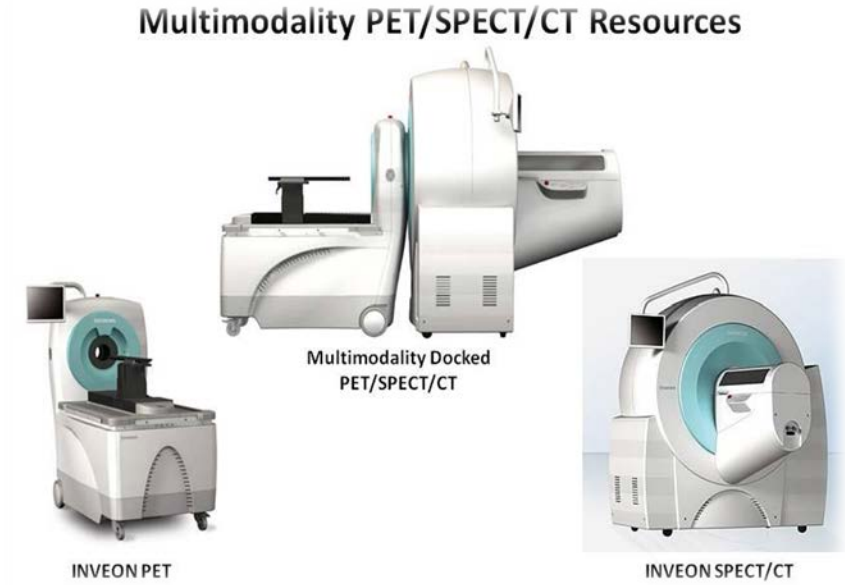
Please Note: All research conducted at the VA BIC must receive prior approval from the appropriate oversight committee(s) including the VA Research and Development Committee, VA Subcommittee for Animal Studies/MU IACUC, VA Subcommittee for Research Safety, or the VA Radiation Safety Committee.

Micro-PET Technology

The Siemens INVEON® PET component of this instrument is equipped with LSO detector technology (1.59 mm X 1.59 mm X 10 mm) allowing rapid data acquisition providing a maximum resolution of 1.4 mm full width half maximum (FWHM) at center field of view. This unit is capable of dedicated stand-alone operation or docking with the INVEON® SPECT / CT for true multimodal data acquisition. Data collection and reconstruction is controlled using a dedicated 64 bit MS Windows platform. Data attenuation correction is provided either through Co-57 transmission source attenuation correction or using CT attenuation correction when operating in docked mode. Data reconstruction algorithms available include 3D-FBP, 2D-OSEM, 3D-RP, 3D-OSEM, 3D-MAP, 3D-OSEM + MAP, and 3D-OSEM + fastMAP™. The resultant reconstructed data is DICOM 3.0 compatible and is ported directly to a Windows based graphical workstation for final image visualization and fusion with data obtained from other imaging modalities (i.e. SPECT / CT / MRI).

Micro-PET technology allows a researcher to monitor the fate of positron emitting probes in an in vivo system. These studies can be performed non-invasively allowing repeated measurements within the same research subject. The predominant use of this instrument is currently in monitoring in vivo tissue metabolism and determining in vivo tissue and cellular viability.

Siemens INVEON® PET



Micro-SPECT Technology

The Siemens INVEON® SPECT component of this instrument is equipped with dual pixellated sodium iodide (NaI) detectors for acquiring high resolution single photon emission computed tomography (SPECT) data. The Micro-SPECT detectors have a high sensitivity (due to a greater pinhole magnification created by the large active area of 150mm x 150mm) which allows for detection of gamma rays from 35 keV to 300 keV. Each detector head is comprised of 4,624 NaI crystals (2 x 2 x 10 mm) arranged in a 68 x 68 crystal array coupled to position sensitive photomultiplier tubes. The system is equipped with 0.5 mm, 1.0 mm, 2.0 mm, and 3.0 mm single pinhole collimators, and 0.5 mm and 1.0 mm multi-pinhole collimators. The SPECT data is collected in a true list mode fashion allowing post acquisition windowing and reconstruction optimization. 3D-OSEM and 3D-MAP are the reconstruction algorithms available for this system. The Micro-SPECT component allows for dynamic planar data acquisition and dual window gating in all acquisition modes.

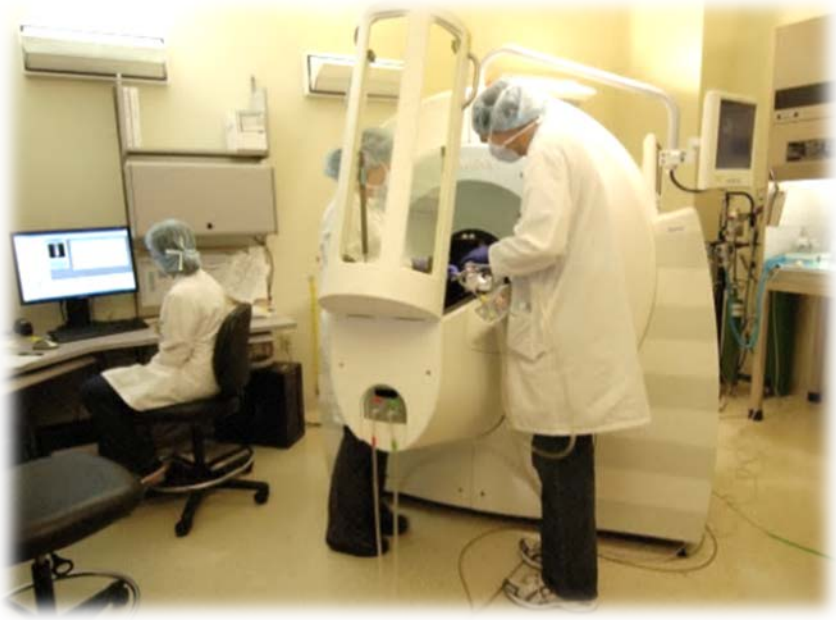
Siemens INVEON® SPECT/CT

Micro-CT Technology

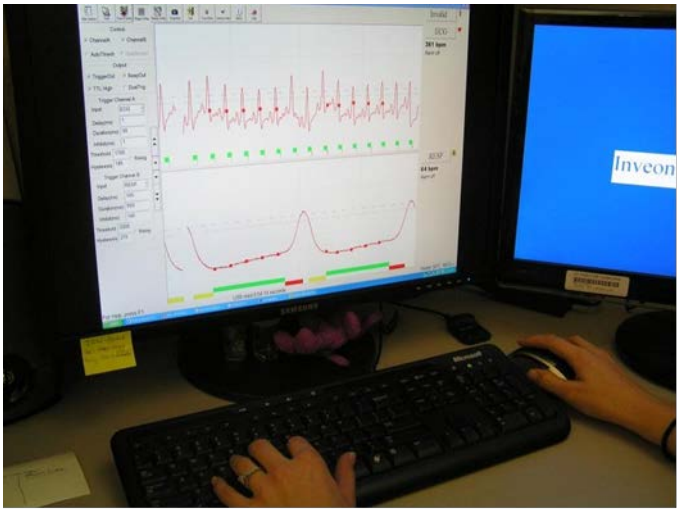
The INVEON® CT component of this instrument is equipped with an 80 kVp x-ray source and appropriate software allowing for the acquisition of single frame x-ray images, fluoroscopic data acquisition, and 360° data acquisition for 3D volume rendered CT data. Fan beam and cone beam (Feldkamp) filtered back projection algorithms are used for reconstructing the CT tomographic images. Reconstruction of Micro-CT data is accomplished on a stand-alone 64 bit MS Window platform.

The combined Micro-CT unit allows the researcher to obtain anatomical data from 3D x-ray computed tomographs and combine this with Micro-SPECT data for accurate identification and localization of drug/metabolite disposition within an in vivo system. Visualization of lesions as small as 0.6 mm in diameter has been achieved using this technology.

Siemens INVEON® SPECT/CT



BioVet™ Physiological Monitoring and Triggering System



BioVet™ (m2m Imaging) default screen.

BioVet™ is a preclinical, physiological monitoring system used for Micro-CT, Micro-SPECT, and Micro-PET imaging. The system is designed to monitor respiratory, temperature, and ECG for purposes of event synchronization. Two physiologic events can be monitored simultaneously while being dependent and/or independent of each other during data acquisitions. By synchronizing the event(s) with the data acquisition, the system is able to minimize motion artifacts which allows image data acquisition gating providing improved lung, brain, and cardiac imaging.

Micro-MRI Technology

Bruker AVANCE III® MRI

The Micro-MRI high performance imaging and spectroscopy system (Bruker BioSpin Corp.) includes a 7 Tesla (T), 210 mm horizontal bore, actively shielded MRI system operated with Bruker Avance III® console and ParaVison® imaging acquisition and processing software. The instrument is equipped with an integrated shim and gradient coil (198 mm /114 mm O.D. /I.D.) with a gradient strength of 450 mT / m, a linear inductive rise time of 110 µs, and a slew rate of 3,680 T / m / s. The instrument is equipped with an SA Physiological Gating Module which provides cardiac and respiratory gating capabilities. The system is further equipped with an actively decoupled ^{1}H volume RF-coil (112 mm O.D. / 86 mm I.D.) combined with a four-element phased-array mouse brain ^{1}H RF-coil, a circularly polarized 35 mm I.D. ^{1}H RF-coil, three quadrature birdcage ^{1}H RF-coils (63 mm I.D.; 38 mm I.D.; 40 mm I.D. millipede), and an assortment of surface RF-coils (^{1}H, ^{31}P). The imaging data is acquired and processed on a Linux HP-Workstation configured for use with ParaVison and TOPSPIN software

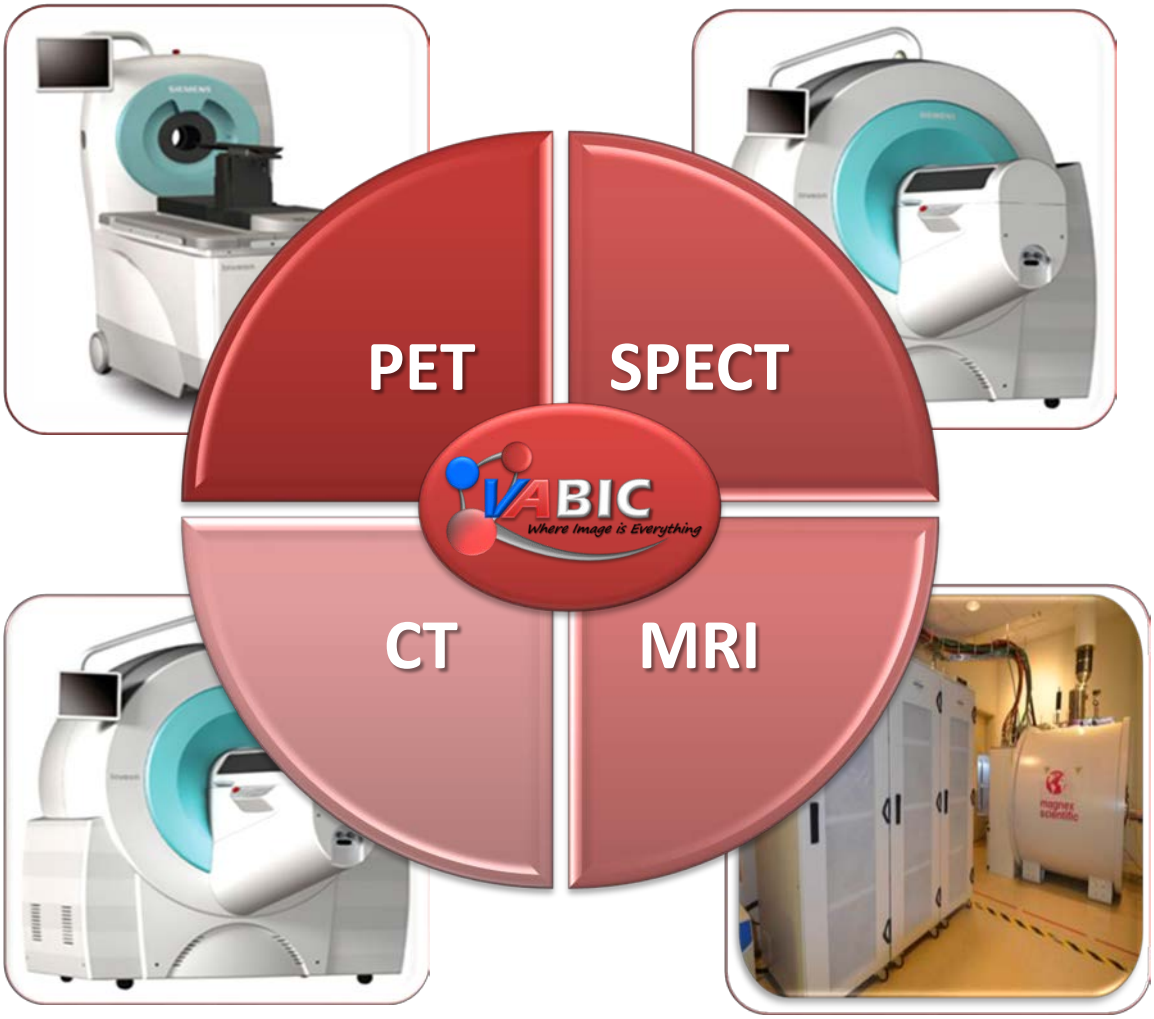
Furthermore, the Micro-MRI system can provide flexibility using tissue contrast options such as T1, T2, T2*, and diffusion weighted imaging. This system has the capability of achieving a 50 µm resolution for brain, cardiac imaging and tumor models.

Because of this instruments capability of producing high resolution anatomical and functional imaging and spectroscopic data in brain, heart, tumor, and other organs in small animal models, it has a wide applicability in a diverse array of research programs including oncology and cardiovascular research.

Currently the available MRI pulse sequences include:

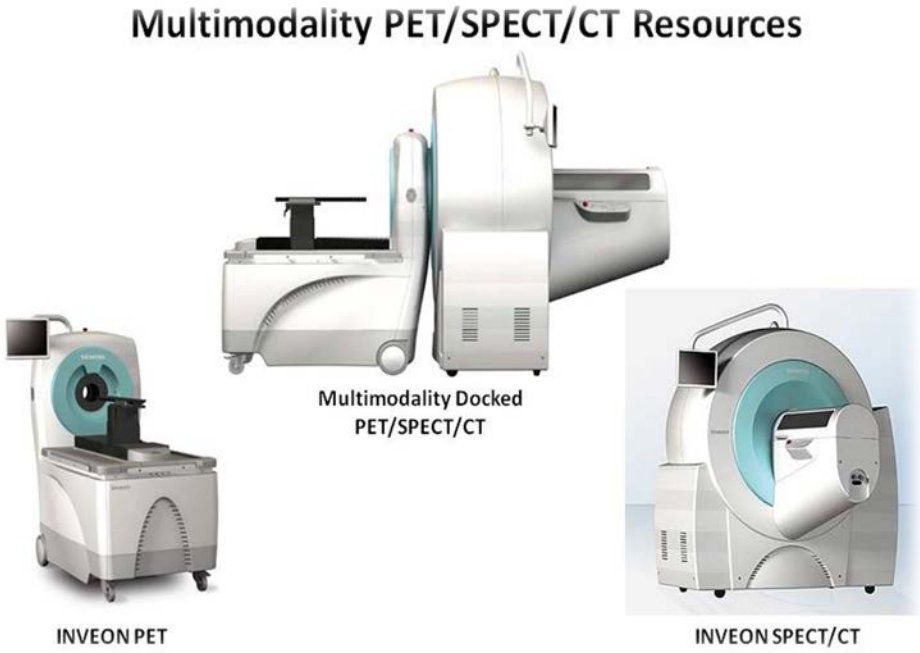
- Multi-slice, multi-echo, 2-dimensional, and 3-dimensional spin-echo T1-weighted, T2-weighted, and proton-density weighted imaging
- Multi-slice, multi-echo, 2-dimensional, and 3-dimensional gradient-echo imaging
- Fast spin echo sequence
- Diffusion-weighted multi-slice imaging sequences (DWI)
- Echo planar imaging (EPI) with gradient-echo and spin-echo options
- Perfusion imaging using pulsed arterial spin labeling
- EPI-DWI
- Parallel imaging
- Diffusion tensor imaging, including calculation tools for tensor component and visualization tools for maps of diffusion direction and tensor components
- Tapped and cine cardiac MRI
- Ultra-short TE (UTE) sequence for short-T2 tissue imaging (i.e. lungs etc.)
- Spiral and partial k-space sequence
- Localized spectroscopy sequences (1H)
- Chemical shift imaging sequence
- MR spectroscopy imaging (MRSI) sequences
- 3D MR angiography
- Steady-state free precession acquisition
- Ability to apply fat suppression, pre-saturation, flow-compensation, magnetization transfer, and inversion-recovery to standard imaging sequences.

Multimodal Technology



Multimodality PET/SPECT/CT & MRI Molecular Imaging Technology

In 2003, the VA BIC was created as a pre-clinical molecular imaging facility. The initial technology acquired at that time included a Philips Mosaic® small animal PET scanner, an ImTEK Micro-SPECT/CT system, and a Varian 7 Tesla small bore MRI. In 2010, the HSTMVH upgraded these facilities as a result of receiving a VA Shared Equipment Enhancement Program (ShEEP) award that provided funds to acquire a Siemens INVEON® Multimodality SPECT/CT system combined with a docking Siemens INVEON® d-PET system. These two systems are capable of either stand-alone operation or docking in a multimodal fashion as shown in the figure below.



In FY2012, the HSTMVH further upgraded the VA BIC preclinical MRI facilities using funds provided by a VA ShEEP award to acquire a Bruker AVANCE III® MRI console. This upgrade was completed in January 2013.

Optical Technology

In Vivo Fluorescence/Bioluminescence Imaging

The Xenogen IVIS® 200 In vivo Fluorescence/Bioluminescence system was purchased by the University of Missouri Radiopharmaceutical Sciences Institute in April of 2005. This instrument is equipped with a cooled CCD camera with 26X26mm field of view and the XFO-12 Fluorescence Module incorporating four standard filter sets and software for autofluorescence background subtraction capabilities. This instrument is capable of monitoring the fate of fluorescent and bioluminescent molecules, probes, and cells in living animals. This technology can be used as both a high throughput screening technology and as a research tool to study the in vivo fate of genetically modified cell lines which express a fluorescent or bioluminescent reporter signal.

IVIS® Imaging System 200

Hot Lab

Synthesis and Purification of Non-Radioactive Peptides

Synthesis and purification of non-radioactive peptides can be performed in the hot lab. Solid phase peptide synthesis is available by using a CEM Liberty® 12 Channel Automated Microwave Peptide Synthesizer (Shown at right). The CEM Liberty® is capable of synthesizing up to 12 peptides per day while unattended at scale range of 0.025 to 5 mmol. The Liberty peptide synthesizer uses microwave energy to expedite peptide synthesis often up making it ten times faster than traditional peptide synthesis methods. HPLC purification of non-radioactive peptides is available using a combination of either Waters or Rainin HPLC systems equipped with a programmable multi-wavelength detector, an auto-sampler, and fraction collecting capability.

CEM Liberty® 12 Automated Peptide Synthesizer

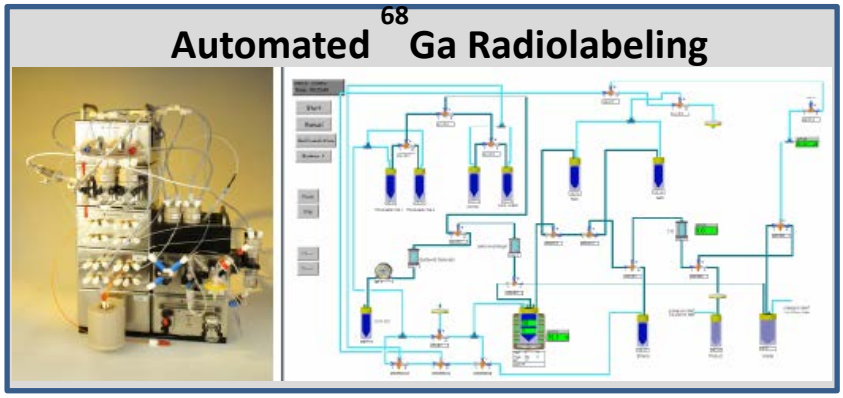
Appropriate radiation prep shields, syringe shields, and sample storage devices are available for handling positron, beta, and gamma emitting radionuclides. The laboratories are secure and equipped with required radiation survey and swipe counter equipment for compliance with current NRC regulations. A separate radiation generator lab is available for secure storage of ^{99}Mo/^{99m}Tc and ^{188}W/^{188}Re generator systems.

.

Hot Cell

Automated Radiosynthesis Technology

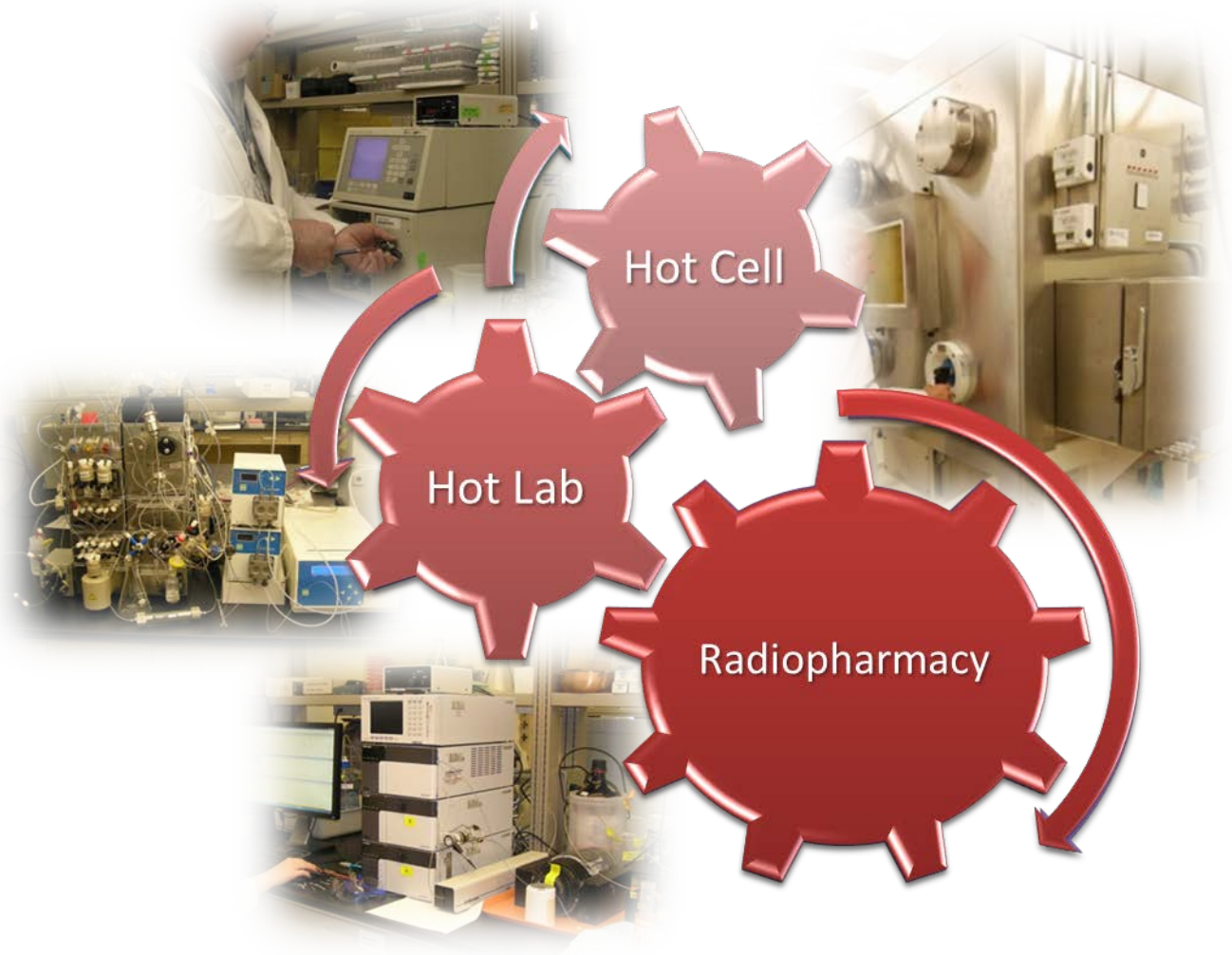
In 2011, the VA BIC installed a ^{68}Ga generator and an Eckert & Ziegler automated ^{68}Ga synthesis system for use in the VA hot cell suite as part of our central radiopharmacy facility for rapid preparation of radiopharmaceuticals for preclinical to clinical translation research for developing diagnostic PET radiopharmaceuticals. An example of the automated synthesis technology and user typical interface are shown in the image on the left.



Radiation Hot Cell Capabilities

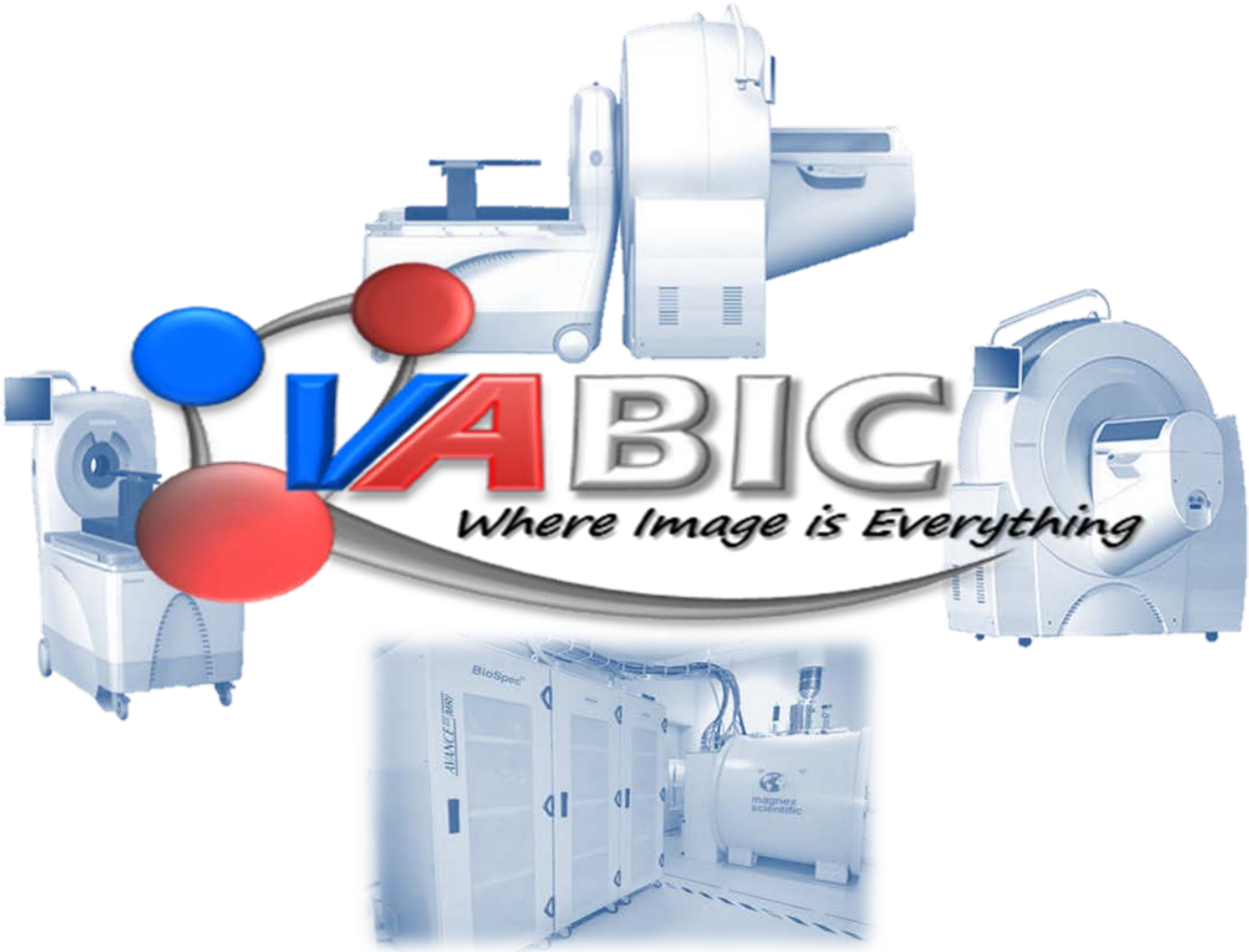
As part of the translational radiopharmaceutical research program at the Truman VA, a dual radiation hot cell is available with ISO 9000 compatible clean room capabilities for the preparation of research grade radiopharmaceuticals. The radiation hot cell is equipped with external manipulator access as well as glove box entry options to provide flexibility in designing and accessing experimental apparatus during synthesis procedures. Dual port access allows both hot cells to be operated and accessed independently permitting the simultaneous synthesis of two radioactive products. The hot cell is also equipped with rear entry opening lead glass windows, dual dose calibrator chamber enclosures all housed within a HEPA filtered suite. An additional vented biosafety cabinet is located within the suite for manual formulation and preparation of sterile products.

Research Radiopharmacy



The preclinical research radiopharmacy provides investigators with automated radiosynthesis of pre-clinical and clinical grade PET and SPECT molecular imaging agents. In order to carry out automated radiosynthesis of molecular imaging agents, the facility is equipped with the appropriate instrumentation to implement synthetic strategies involving the use of high energy positron and gamma emitting radioactive materials, as well as, the personnel with the required expertise in radiochemical and radiopharmaceutical development.

Contact Information



For additional information or to speak with a representative of the VA-BIC imaging facility, please call the Harry S. Truman Memorial Veterans' Hospital's research and development office at 1-573-814-6550.